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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,124	09/26/2003	Hidetoshi Inoko	ORIN-003CIP	2646

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EXAMINER	
O FARRELL, THOMAS JOHN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/674,124	INOKO ET AL.	
	Examiner	Art Unit	
	Thomas J. O'Farrell	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *5-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/18/04, 06/25/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group 1, with the election of the combination of SEQ ID NO:1 and 2 in claim 3, in the reply filed on 11/16/2005 is acknowledged. The traversal is on the ground(s) that it is not clear as to whether the sequence election for claim 3 is an election of species. This is not found persuasive because the examiner notes that the sequence election in claim 3 is not an election of species but an election of distinct inventions. Nucleotide sequences encoding different proteins or other polynucleotides that have nucleotide sequences are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence are presumed to represent an independent and distinct invention, subject to restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141. By statute, "[i]f two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions." 35 U.S.C. 121. Pursuant to this statute, the rules provide that "[i]f two or more independent and distinct inventions are claimed in a single application, the examiner in his action shall require the applicant... to elect that invention to which his claim shall be restricted." 37 CFR 1.142 (a). See also

37 CFR 1.141(a). It is noted that searching more than one specific set of the claimed patentably distinct sequences represents a serious burden for the office.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-4 are currently under consideration. An action on the merits follows. Claims 5-12 are withdrawn as being drawn to non elected inventions.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on 04/13/2000. It is noted, however, that applicant has not filed a certified copy of the 2000-112699 application as required by 35 U.S.C. 119(b). Therefore priority to the 2000-112699 application has not been granted to the instantly pending claims.

4. Acknowledgment is made of applicant's claim for foreign priority based on applications filed in Japan on 09/28/2002 and 12/09/2002. It is noted, however, that applicant has not filed certified translated copies of the 2002-327516 and 2002-383869 applications. Therefore priority to the 2002-327516 and 2002-383869 applications has not been granted to the instantly pending claims.

5. The instant application is a continuation-in-part of US application serial no. 10/257,511, filed march 7, 2003, which application is a §371 national phase application of PCT/JP00/07621, filed 10/30/2000. Claim 2 is not supported and claim 3 is not supported with respect to the SEQ ID NO:'s recited in claim 3. Therefore, claims 2 and 3 are awarded the effective filing date of 09/26/03, the filing date of the instant application.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 3 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The method of gene mapping entailing amplification of a combination of microsatellite markers comprising SEQ ID NO:'s 1 and 2 from interest and control subjects and comparing the DNA fragments produced where comparing indentifies DNA fragments with one or more genomic regions associated with the characteristic of interest is not supported by a specific asserted utility because the specification does not teach an association between the microsatellite markers of SEQ ID NO:'s 1 and 2 and any specific phenotype or specific gene associated with a phenotype and therefore the use of these markers in the disclosed method of gene mapping is not expected to have

any specific effect. The specification teaches that the invention involves a gene mapping method which entails analysis of a DNA sample from test and control subjects for the presence of an allelic form of a plurality of microsatellite markers in order to identify regions of the genome associated with a characteristic of the test subject relative to the control subjects such as a region containing a pathogenic gene (page 3, para 0010). The specification teaches that SEQ ID NO:'s 1 and 2 are genetic polymorphism markers and are located on chromosome 1 (page 6, para 0045 and 0046). The specification teaches that 6 markers located on chromosome 1 were found to be associated with rheumatoid arthritis (page 60, para 00248). However, the specification does not teach an association between the microsatellite markers of SEQ ID NO:'s 1 and 2 and any specific phenotype or specific gene associated with a phenotype and therefore the use of these markers in the disclosed method of gene mapping is not expected to have any predictable or specific effect.

The method of gene mapping entailing amplification of a combination of microsatellite markers comprising SEQ ID NO:'s 1 and 2 from interest and control subjects and comparing the DNA fragments produced where comparing indentifies DNA fragments with one or more genomic regions associated with the characteristic of interest is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. The specification teaches that SEQ ID NO:'s 1 and 2 and the other microsatellite polymorphisms disclosed can be used in the claimed method to identify regions containing pathogenic genes or genes relating to human phenotypes with genetic factors (see page 3, para 0010). The specification

teaches that susceptibility genes within these regions can be identified by further SNP analysis (page 60, para 00249). The specification teaches that genes isolated by the claimed method, proteins encoded by these genes, antibodies against the proteins, and/or polynucleotides containing at least 15 nucleotides complementary to one of the strands of these genes or their complementary strands may be used for genetic screening and gene therapy (page 60, para 00250). Furthermore, the specification teaches that a pathogenic gene of a disease isolated by the claimed method, proteins encoded by these genes, antibodies against the proteins, and/or polynucleotides containing at least 15 nucleotides complementary to one of the strands of these genes or their complementary strands may be used for testing, preventing, and/or treating the disease (see page 60, para 00250). However, a starting material that can only be used to produce a final product does not have a substantial utility where the product is not supported by a specific and substantial utility. In the instant case, the genes identified that could possibly be identified by the use of SEQ ID NO: 1 and 2 in the claimed method are not taught by the specification nor are they known in the art and therefore the use of SEQ ID NO:'s 1 and 2 to identify such genes does not constitute a substantial or "real world" utility. Therefore, because the specification and the art does not teach an association between the microsatellite markers of SEQ ID NO:'s 1 and 2 and any specific phenotype or specific gene associated with a particular phenotype, no substantial utility is provided for the use of SEQ ID NO: 1 and 2 in the claimed method of gene mapping.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 3 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The claim is drawn to a method of gene mapping entailing amplification of a combination of microsatellite markers comprising SEQ ID NO:'s 1 and 2 from interest and control subjects and comparing the DNA fragments produced where comparing indentifies DNA fragments with one or more genomic regions associated with the characteristic of interest. The specification teaches that SEQ ID NO:'s 1 and 2 and the other microsatellite polymorphisms disclosed can be used in the claimed method to identify regions containing pathogenic genes or genes relating to human phenotypes with genetic factors (see page 3, para 0010). The specification teaches that susceptibility genes can be identified by further SNP analysis (page 60, para 00249). The specification teaches that genes isolated by the claimed method, proteins encoded by these genes, antibodies against the proteins, and/or polynucleotides containing at least 15 nucleotides complementary to one of the strands of these genes or their

complementary strands may be used for genetic screening and gene therapy (page 60, para 00250). Furthermore, the specification teaches that a pathogenic gene of a disease isolated by the claimed method, proteins encoded by these genes, antibodies against the proteins, and/or polynucleotides containing at least 15 nucleotides complementary to one of the strands of these genes or their complementary strands may be used for testing, preventing, and/or treating the disease (see page 60, para 00250). However, the specification nor the art teaches any association, nor a predictable association, between the microsatellite markers of SEQ ID NO:'s 1 and 2 and any specific phenotype or specific gene associated with a particular phenotype. In addition, the art and the specification teaches that although many microsatellite polymorphisms exist in the human genome, not all are linked to a particular gene or region of the genome that is associated with a particular phenotype. The skilled artisan would have to test for a predictable association between SEQ ID NO:'s 1 and 2 and a region of the genome or specific gene associated with a phenotype by the claimed method which would involve testing many different regions of the genome or genes associated with many different phenotypes and may not lead to success and, therefore, this would be considered undue experimentation as it would involve unpredictable trial and error analysis. Because the specification nor the art has taught a predictable association between the microsatellite markers of SEQ ID NO:'s 1 and 2 and any specific phenotype or specific gene associated with a particular phenotype, undue and unpredictable experimentation would be required of the skilled artisan to determine how to use the claimed invention

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barcellos et al. (herein referred to as Barcellos, 1997, Am. J. Hum. Genet., vol. 61, pages 734-747) in view of Kamb (herein referred to as Kamb, US Patent 5683880, 11/1887).

Barcellos teaches a method of using pooled DNA amplifications of microsatallite markers to facilitate the efficient, cost-effective, high-resolution genome screening for detection of disease loci by association (see page 735, column 2, para 2, lines 1-4 of Barcellos). Barcellos teaches that this method involves collecting DNA from control and interest subjects (see page 735, all of last para and page 736 all of first para of Barcellos), pooling the DNA from the control and interest populations (claim 2; see page 736, para 21, lines 13-17 of Barcellos), amplifying fragments containing microsatellite markers in particular parts of the genome (see page 736, column 1, all of para 3 of Barcellos), comparing the abundance of the fragments from the control and test subjects with statistical methods including AFBAC, stutter correction, and preferential amplification correction to achieve allele frequencies and also using multiple comparisons with independent amplifications (see page 736, column 2, all of para 2, page 737, all of para 2, page 738 column 1, lines 9-12, Table 1, and Figure 2 of Barcellos), where an increased frequency of a particular allele in the test population indicates an association of that allele and the phenotype of the test population (see page 737, all of para 4, and page 738, all of para 1, and Figure 2 of Barcellos).

Barcellos does not teach in the method of high-resolution genome screening entailing the amplification of microsatellite markers in the genome taught by Barcellos, the *specific* distances between the microsatellite markers chosen for the analysis. However, Kamb teaches that microsatellite repeats are located in the human genome at intervals of approximately 100 kb (see column 1, lines 57-67 and column 2 lines 1-10 of Kamb). Therefore, it would have been prima facie obvious to one of ordinary skill in the

art at the time the invention was made to practice the method of high-resolution genome screening for detection of disease loci entailing the amplification of microsatellite markers in the genome taught by Barcellos by amplifying microsatellite markers that are 50-150 kb apart in the genome in view of the teachings of Kamb. The ordinary artisan would have been motivated to practice the method of high-resolution genome screening for detection of disease loci entailing the amplification of microsatellite markers in the genome by amplifying microsatellite markers that are 50-150 kb apart in the genome because Kamb teaches that microsatellite repeats are located in the human genome at intervals of approximately 100 kb.

13. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baracellos in view of Kamb as applied to claim 1 above, and further in view of Braun (herein referred to as Braun, 1997, Genomics, vol. 46, pages 18-23).

The teachings of Baracellos in view of Kamb as applied to claim 1 are recited in para 12 above.

Baracellos in view of Kamb do not teach a method of high-resolution genome screening entailing the amplification of microsatellite markers in the genome where the microsatellite markers are analyzed by a DNA chip and a mass spectrometer. However, Braun teaches that amplified DNA containing microsatellite markers can be analyzed for its size by applying the amplified DNA to a probe target disk, interpreted as a DNA chip, and subsequent analysis by a mass spectrometer (see page 19, column 1, all of para 4 and 5, and column 2, all of para 1 and 2, and Figure 1 of Braun). Braun

teaches that this method of analyzing microsatellites using a probe target disk and mass spectrometer achieves highly accurate sizing of microsatellites (see page 19, column 1, para 1, lines 1-4 of Braun). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze the amplified microsatellite regions in the method of high-resolution genome screening for detection of disease loci entailing the amplification of microsatellite markers and analysis of the sizes of the amplified markers taught by Barcellos in view of Kamb by using a probe target disk and mass spectrometry in view of the teachings of Braun. The ordinary artisan would have been motivated to analyze the amplified microsatellite regions in the method of high-resolution genome screening for detection of disease loci entailing the amplification of microsatellite markers and analysis of the sizes of the amplified markers taught by Barcellos in view of Kamb by using a probe target disk and mass spectrometry because Braun teaches that the method of analyzing the sizes of amplified DNA containing microsatellite markers using a probe target disk and mass spectrometry achieves highly accurate sizing of microsatellites.

14. Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kamb.

Kamb teaches a method of localizing a gene associated with a disease to a small region of a chromosome by associating the gene with a microsatellite marker(s) (see column 2, lines 30-34 and column 3, lines 19-21 of Kamb). Kamb teaches that this method entails obtaining DNA form normal and interest subjects (see column 4, lines

63-64), amplifying microsatellite markers by using primers that are complimentary to each side of the markers where the primers can have different colored labels (see column 2, lines 39-48 of Kamb), and separating the amplified DNAs by size by electrophoresis and recording the intensities of each amplified fragment to give the relative amount of each fragment (see column 2, lines 55-64 of Kamb). Kamb teaches that a difference spectrum is then determined by normalizing the signal from the control individuals with the signal from the interest individuals to produce scaled control and interest signals and subtracting the control signal from the interest signal, interpreted as statistically comparing the amplified fragments (see column 2, lines 63-65, and column 3, lines 61-65 of Kamb). Kamb teaches that a peak in the difference spectrum indicates that a particular marker is associated with the interest subjects (see column 3, lines 3-6 and 48-49 of Kamb). Kamb teaches that the DNA from the control and the test populations can be pooled before amplification (claim 2; see column 2, lines 48-52 and column 5, lines 14-19 of Kamb).

Kamb does not teach a method of localizing a gene associated with a disease to a small region of a chromosome by associating the gene with microsatellite markers, *specifically* where the microsatellite markers analyzed are located at intervals of from about 50-150 kb in the human genome. However, Kamb teaches that microsatellite repeats are located in the human genome at intervals of approximately 100 kb (see column 1, lines 57-67 and column 2 lines 1-10 of Kamb). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze microsatellite markers that are located at intervals of from about 50-150 kb in

the human genome in the method of localizing a gene associated with a disease to a small region of a chromosome by associating the gene with microsatellite markers taught by Kamb in view of the teachings of Kamb. The ordinary artisan would have been motivated to analyze microsatellite markers that are located at intervals of from *about 50-150 kb* in the human genome in the method of localizing a gene associated with a disease to a small region of a chromosome by associating the gene with microsatellite markers taught by Kamb because Kamb teaches that microsatellite repeats are located in the human genome at intervals of approximately 100 kb.

15. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kamb as applied to claim 1 above, and further in view of Braun.

The teachings of Kamb as applied to claim 1 are recited in para 14 above.

Kamb does not teach a method of localizing a gene associated with a disease to a small region of a chromosome by associating the gene with microsatellite markers, *specifically* where the analysis of the amplified microsatellite DNA is carried out by a DNA chip and a mass spectrometer. However, Braun teaches that amplified DNA containing microsatellite markers can be analyzed for its size by applying the amplified DNA to a probe target disk, interpreted as a DNA chip, and subsequent analysis by a mass spectrometer (see page 19, column 1, all of para 4 and 5, and column 2, all of para 1 and 2, and Figure 1 of Braun). Braun teaches that this method of analyzing microsatellites using a probe disk and mass spectrometer achieves highly accurate sizing of microsatellites (see page 19, column 1, para 1, lines 1-4 of Braun). Therefore,

it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze the amplified microsatellite DNAs in the method of localizing a gene associated with a disease to a small region of a chromosome by associating the gene with microsatellite markers taught by Kamb
by using a probe target disk and mass spectrometry in view of the teachings of Braun. The ordinary artisan would have been motivated to analyze the amplified microsatellite DNAs in the method of localizing a gene associated with a disease to a small region of a chromosome by associating the gene with microsatellite markers taught by Kamb
by using a probe target disk and mass spectrometry because Braun teaches that the method of analyzing the sizes of amplified DNA containing microsatellite markers using a probe target disk and mass spectrometry achieves highly accurate sizing of microsatellites.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas O'Farrell whose telephone number is (571) 272-8782. The examiner can normally be reached Monday-Friday from 8:30 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Thomas O'Farrell
Examiner
Art Unit 1634

1/21/06

JEHANNE SITTON
PRIMARY EXAMINER
1/30/06